#10 Attachment
09/891138

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

INVITATION TO PAY ADDITIONAL FEES

(PCT Article 17(3)(a) and Rule 40.1)

To:
TOWNSEND AND TOWNSEND AND CREW LLP
Attn. Lockyer, Jean M.
Two Embarcadero Center
Eighth Floor
San Francisco, CA 94111
UNITED STATES OF AMERICA

RECOMMANDEE

Date of mailing *(day/month/year)*	19/07/2002
Applicant's or agent's file reference 18781-62-1PC	**PAYMENT DUE** 9-02-02 within 45 ~~months~~/days from the above date of mailing
International application No. PCT/US 01/ 20363 J	International filing date *(day/month/year)* 25/06/2001 √

Applicant

TULARIK INC. et al. J

1. This International Searching Authority

(i) considers that there are 8 *(number of)* inventions claimed in the international application covered by the claims indicated ~~below~~/on the extra sheet:

and it considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated ~~below~~/on the extra sheet:

(ii) [X] has carried out a partial international search (see Annex) [ ] will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.:

1-12,21-28,34-52,70-75 (all partially)

(iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid

2. The applicant is hereby **invited,** within the time limit indicated above, to pay the amount indicated below:

EUR 945,00	x	7	=	EUR 6.615,00
Fee per additional invention		number of additional inventions		total amount of additional fees

Or, _____ x _____ = _____

The applicant is informed that, according to Rule 40.2(c), **the payment of any additional fee may be made under protest,** i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. [X] Claim(s) Nos. further info _____ have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the International Searching Authority	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Henriëtte Huysing-Solles

Form PCT/ISA/206 (July 1992)

FEES DUE 9-02-02
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This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-12, 21-28, 34-52, 70-75 (all partially)

   the isolated G protein-coupled receptor having the amino acid sequence SEQ ID NO: 6, isolated nucleic acids encoding said protein, vectors and host cells containing these nucleic acids, methods for the identification of modulators of said protein and methods for the detection of said protein or the nucleic acids encoding it

2. Claims: 1-12, 21-28, 34-52, 70-75 (all partially)

   the isolated G protein-coupled receptor having the amino acid sequence SEQ ID NO: 4, isolated nucleic acids encoding said protein, vectors and host cells containing these nucleic acids, methods for the identification of modulators of said protein and methods for the detection of said protein or the nucleic acids encoding it

3. Claims: 1-12, 21-28, 34-52, 70-75 (all partially)

   the isolated G protein-coupled receptor having the amino acid sequence SEQ ID NO: 8, isolated nucleic acids encoding said protein, vectors and host cells containing these nucleic acids, methods for the identification of modulators of said protein and methods for the detection of said protein or the nucleic acids encoding it

4. Claims: 1-12, 21-28, 34-52, 70-75 (all partially)

   the isolated G protein-coupled receptor having the amino acid sequence SEQ ID NO: 10, isolated nucleic acids encoding said protein, vectors and host cells containing these nucleic acids, methods for the identification of modulators of said protein and methods for the detection of said protein or the nucleic acids encoding it

5. Claims: 1-12, 21-28, 34-52, 70-75 (all partially)

   the isolated G protein-coupled receptor having the amino acid sequence SEQ ID NO: 12, isolated nucleic acids encoding said protein, vectors and host cells containing these nucleic acids, methods for the identification of modulators of said protein and methods for the detection of said protein or the nucleic acids encoding it

6. Claims: 1-12, 21-28, 34-52, 70-75 (all partially)

   the isolated G protein-coupled receptor having the amino acid sequence SEQ ID NO: 16, isolated nucleic acids encoding said protein, vectors and host cells containing these nucleic acids, methods for the identification of modulators of said protein and methods for the detection of said

protein or the nucleic acids encoding it

7. Claims: 13, 19, 29, 53, 67-69 (all completely), 15-18, 31-36, 55-66, 74, 75 (all partially)

the isolated G protein-coupled receptor having the amino acid sequence SEQ ID NO: 2, isolated nucleic acids encoding said protein, vectors and host cells containing these nucleic acids, methods for the identification of modulators of said protein and methods for the detection of said protein or the nucleic acids encoding it

8. Claims: 14, 20, 30, 54 (all completely), 15-18, 31-36, 55-66, 74, 75 (all partially)

the isolated G protein-coupled receptor having the amino acid sequence SEQ ID NO: 14, isolated nucleic acids encoding said protein, vectors and host cells containing these nucleic acids, methods for the identification of modulators of said protein and methods for the detection of said protein or the nucleic acids encoding it

The following documents are considered to be relevant for the assessment of the unity of the invention:

D1: STADEL J M et al. "Orphan G protein-coupled receptors: a neglected opportunity for pioneer drug discovery", TRENDS IN PHARMACOLOGICAL SCIENCES, November 1997, vol. 18, pages 430-437.
D2: WO 00 31258, 2 June 2000

D1 describes the pharmaceutical potential of G protein-coupled receptors, while D2 discloses several G protein-coupled receptors, inter alia one receptor (SEQ ID NO: 13 and 14), which is 100% identical to the receptor having the amino acid sequence SEQ ID NO: 6.

In the light of these prior art documents D1 and D2, the problem underlying the present application is to provide alternative or further G protein-coupled receptors.
The present application offers 8 solutions to this problem, as outlined in more detail above.

The single general concept covering all separate inventions is, according to the description, page 1, the notion that all the provided sequences encode G protein-coupled receptors, which are useful in drug discovery and disease diagnosis.

This concept is known in the state of the art. As described in D1, G protein-coupled receptors are important therapeutic targets. A non-exhaustive list of receptors is shown in table 1 of D1.

This takes away the linking concept possibly unifying the groups of inventions claimed in the present application.

As the single general concept is not novel it cannot be the single general inventive concept required to be present by Article 3(4)(iii) and Rule 13.1 PCT. When considering the whole set of claims in the light of the description no further technical features could be identified which could serve as same or corresponding technical features in the sense of Rule 13.2 PCT to restore unity of invention.

As prescribed in Article 17(3)(a) PCT, the invention first mentioned in the claims (subject 1, claims 1-12, 21-28, 34-52, 70-75, all partially) has been the subject of the search. The subjects 2-8 are not mutually linked by a further general inventive concept and searching each subject requires a major search effort.
Consequently, this invitation to pay additional fees has been formulated in accordance with Article 17(3)(a) PCT.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 206

Continuation of Box 3.

Although claims 67 to 73 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Further defect(s) under Article 17(2)(a):

Continuation of Box 3.

Present claims 67 to 74 relate to products, defined by reference to a desirable characteristic or property, namely their property to interact with the disclosed G-protein coupled receptors and subsequently modulate signal transduction processes (claims 67 to 73), and their selective association with said receptor or the nucleic acid encoding said receptor (claim 74), respectively.

The claims cover all products and methods having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such products and methods. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product/method by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to antibodies, oligonucleotide primers and nucleic acid probes, as mentioned in claim 75.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

Annex to Form PCT/ISA/206
COMMUNICATION RELATING TO THE RESULTS OF THE PARTIAL INTERNATIONAL SEARCH

International Application No
PCT/US 01/20363

1. The present communication is an Annex to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:
see 'Invitation to pay additional fees'
2. This communication is not the international search report which will be established according to Article 18 and Rule 43.

3. If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.

4. If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 31258 A (ARENA PHARMACEUTICALS INC; LIAW CHEN W (US); LIN I LIN (US); CHEN) 2 June 2000 (2000-06-02) the whole document, in particular SEQ ID NO: 13 & 14	1-12, 21-28, 34-52, 70-75
X	WO 00 22131 A (ARENA PHARMACEUTICALS INC; GORE MARTIN (US); LIAW CHEN W (US); LIN) 20 April 2000 (2000-04-20) SEQ ID NO: 13 & 14	1-12, 21-28, 34-52, 70-75
P,X	WO 01 33221 A (MICHALOVICH DAVID; SMITHKLINE BEECHAM PLC (GB); SMITHKLINE BEECHAM) 10 May 2001 (2001-05-10) SEQ ID NO: 1 & 2	1-12, 21-28, 34-52, 70-75
P,X	EP 1 096 009 A (PFIZER LTD ;PFIZER (US)) 2 May 2001 (2001-05-02) SEQ ID NO: 1 & 2	1-12, 21-28, 34-52, 70-75
P,X	WO 01 25432 A (SCHERING CORP) 12 April 2001 (2001-04-12) SEQ ID NO: 1 & 2	1-12, 21-28, 34-52, 70-75
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

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Form PCT/ISA/206 (Annex, first sheet) (July 1992)

International Application No
PCT/US 01/20363

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
E	WO 01 46414 A (BANYU PHARMA CO LTD ;OHTA MASATAKA (JP); ITADANI HIRAKU (JP); NAKA) 28 June 2001 (2001-06-28) SEQ ID NO: 1 & 2	1-12, 21-28, 34-52, 70-75
E	WO 01 85793 A (LIND PETER ;SEJLITZ TORSTEN (SE); UPJOHN CO (US); VOGELI GABRIEL ()) 15 November 2001 (2001-11-15) SEQ ID NO: 1 & 2	1-12, 21-28, 34-52, 70-75
A	STADEL J M ET AL: "Orphan G protein-coupled receptors: a neglected opportunity for pioneer drug discovery" TRENDS IN PHARMACOLOGICAL SCIENCES, ELSEVIER TRENDS JOURNAL, CAMBRIDGE, GB, vol. 18, no. 11, 1 November 1997 (1997-11-01), pages 430-437, XP004099345 ISSN: 0165-6147 the whole document	1-12, 21-28, 34-52, 70-75

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Patent Family Annex

Information on patent family members

International Application No
PCT/US 01/20363

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0031258 A	02-06-2000	AU 3790400 A	13-06-2000
		CN 1344319 T	10-04-2002
		EP 1137776 A2	04-10-2001
		EP 1133559 A2	19-09-2001
		WO 0031258 A2	02-06-2000
		WO 0022131 A2	20-04-2000
		AU 6299199 A	01-05-2000
WO 0022131 A	20-04-2000	AU 6299199 A	01-05-2000
		AU 6430799 A	01-05-2000
		DE 1121431 T1	23-05-2002
		EP 1137776 A2	04-10-2001
		EP 1121431 A1	08-08-2001
		ES 2163384 T1	01-02-2002
		WO 0021987 A2	20-04-2000
		WO 0022129 A1	20-04-2000
		WO 0022131 A2	20-04-2000
		AU 3790400 A	13-06-2000
		CN 1344319 T	10-04-2002
		EP 1133559 A2	19-09-2001
		WO 0031258 A2	02-06-2000
WO 0133221 A	10-05-2001	WO 0133221 A1	10-05-2001
EP 1096009 A	02-05-2001	EP 1096009 A1	02-05-2001
		GB 2356864 A	06-06-2001
		JP 2001211889 A	07-08-2001
WO 0125432 A	12-04-2001	US 6204017 B1	20-03-2001
		AU 1073501 A	10-05-2001
		WO 0125432 A2	12-04-2001
WO 0146414 A	28-06-2001	AU 2398501 A	03-07-2001
		WO 0146414 A1	28-06-2001
WO 0185793 A	15-11-2001	AU 5961201 A	20-11-2001
		WO 0185793 A2	15-11-2001